UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/802,232 | 03/08/2001 | Yoshihiko Makino | JG-YY-5052 / 500569.2 | 6671 |

26418 7590 07/26/2002

REED SMITH LLP
375 PARK AVENUE
NEW YORK, NY 10152

| EXAMINER | |
|---|---|
| LU, FRANK WEI MIN | |
| ART UNIT | PAPER NUMBER |
| 1634 | |

DATE MAILED: 07/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/802,232 | Makino, Y. | |
| | Examiner | Art Unit | |
| | Frank Lu | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *20 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action* .

## DETAILED ACTION

### *Response to Amendment*

1. Applicant's response to the office action and priority paper filed on May 20, 2002 has been entered as Paper Nos: 4 and 5. The claims pending in this application are claims 1-20. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn.

### *Claim Rejections - 35 USC § 102/103*

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 2, 5-12, and 15-20 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Piunno *et al.,* (Anal. Chem., 67, 2635-2643, August 1995).

. Piunno *et al.,* teach a fiber-optical DNA sensor for fluorometric nucleic acid determination.

Regarding claims 1, 2, 9-12, 19, and 20, Piunno *et al.,*teach to detect the association and dissociation of immobilized dT20 with dA20, rA20 and noncomplement DNA (dR19). The hybridization (forming double stranded complexes) between dT20 immobilized on a optical fiber (an oligonucleotide probe molecule on a solid carrier recited in claims 1, 10, 11, and 20), and dA20, rA20 and noncomplement DNA (dR19) were monitored by the use of the fluorescent DNA stain ethidium bromide and the dissociation of these double stranded complexes were determined by their melting curve (variation of temperature recited in claims 2 and 12) and monitored using UV-visible spectrometer (see abstract in page 2635, page 2639, Figures 3 , 5, and 6, and Table 1 in pages 2641 and 2642). Note that dA 20 could be considered as a sample nucleic acid while rA20 could be considered as a reference nucleic acid recited in claims 1 and 11.

Regarding claims 5, 6, 15, and 16, ethidium bromide could be considered as the labeled intercalator having an electroconductive and fluorescent properties since a nucleic acid -ethidium bromide complex had fluorescence and could transfer electrons.

Regarding claims 7, 8, 17, and 18, dT20 could be considered as the probe molecule that contained a chain of a base sequence comprising at least three predetermined base units in series while rA20 could be considered as the reference nucleic acid wherein its fragment contained a chain of a base sequence comprising at least three predetermined base units in series which were fully complementary to the chain of the probe molecule since both dT20 and rA20 had 20 bp nucleotide and their sequence had known.

Although Piunno *et al.,* do not directly show to compare the stability between the sample and reference double stranded nucleic acid complexes, they detected the dissociation of double stranded nucleic acids by measuring decrease of quantity of the labeled intercalator on the solid carrier recited in claim 1 (see left column in page 2639, 2642, and 2643). Therefore, in the absence of convincing evidence to the contrary, this limitation was considered to be inherent to the reference taught by Piunno *et al.,* since Piunno *et al.,* could know the stability between the sample and reference double stranded nucleic acid complexes during the process of measuring decrease of quantity of the labeled intercalator on the optical fiber.

Alternatively, if applicant argues that Piunno *et al.,* do not show to compare the stability between the sample and reference double stranded nucleic acid complexes recited in claims 1 and 11 and ethidium bromide is not an electroconductive label recited in claims 5 and 15, the examiner noted that Piunno *et al.,* measured the dissociation of these double stranded complexes using their melting curve (see above) wherein the fraction of single stranded nucleic acid on the optical fiber in different temperatures could indicate how stability a double stranded nucleic acid complex was (see Figure 3 in page 2641) and the electroconductive intercalators for the

electrochemical analysis of nucleic acid was known in the art (see page 12 of the specification and for an example, see Takenaka *et al.,* Chem. Commun., 10, 111 and 1112, 1998). Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected the dissociation of double stranded nucleic acids and compared the stability between the sample and reference double stranded nucleic acid complexes by measuring decrease of quantity of the labeled electroconductive intercalator on the solid carrier. One having ordinary skill in the art would have motivated to modify the methods of Piunno *et al.*, because the detection of the dissociation of a double stranded nucleic acid using its melt curve was known in the art at the time the invention was made and the simple replacement of a known method (using a melting curve) from another known method (measuring decrease of quantity of the labeled intercalator) for monitoring the dissociation and stability of a double stranded nucleic acid, and the simple replacement of one labeled intercalator with known properties (i.e., ethidium bromide) from another labeled intercalator with known properties (i.e., an electroconductive intercalator) would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

5. Claims 4 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piunno *et al.,* (1995) as applied to claims 1, 2, 5-12, and 15-20 above.

The teachings of Piunno *et al.,* have been summarized previously, *supra.* Although Piunno *et al.,* did not directly disclose to dissociate double stranded nucleic acids in the presence of varied ionic strengths, Piunno *et al.*, did suggest that the duplex stability in low ionic strength buffers was less than that in high ionic strength buffers (see left column in page 2641).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected the dissociation of double stranded nucleic acids and compared the stability between the sample and reference double stranded nucleic acid complexes in the presence of varied ionic strengths. One having ordinary skill in the art would have motivated to modify the methods of Piunno *et al.*, because it was known in the art at the time the invention was made that the duplex stability in low ionic strength buffers is less than that in high ionic strength buffers, and the simple replacement of a known method (using varied temperature) from another known method (using varied ionic strength) for monitoring the dissociation and stability of a double stranded nucleic acid would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

6. Claim 3 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piunno *et al.,* (1995) as applied to claims 1, 2, 4-12, and 14-20 above, and further in view of Sosnowski *et al.,* (US Patent No. 6,051,380, filed on December 5, 1997).

The teachings of Piunno *et al.,* have been summarized previously, *supra.*

Piunno *et al.,* did not disclose to dissociate double stranded nucleic acids using varied electrophoretic potential.

Sosnowski *et al.,* do teach to electronically denature double stranded nucleic acids. Note that polarity at microlocation in a self-assembling microelectronic device was reversed and voltage was applied to separate the two strands (see columns 60 and 61).

Therefore, in the absence of an unexpected result, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to have detected the dissociation of double stranded nucleic acids and compared the stability between the sample and reference double stranded nucleic acid complexes using varied electrophoretic potential. One

having ordinary skill in the art would have motivated to modify the methods of Piunno *et al.*, because it was known in the art at the time the invention was made that double stranded nucleic acids could be electronically separation by denaturation and the simple replacement of a known method (using varied temperature) from another known method (using varied electrophoretic potential) for monitoring the dissociation and stability of a double stranded nucleic acid would have been, in the absence of an unexpected result, *prima facie* obvious to one having ordinary skill in the art at the time the invention was made.

Furthermore, the motivation to make the substitution cited above arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making the obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

Also note that there is no invention involved in combining old elements is such a manner that these elements perform in combination the same function as set forth in the prior art without giving unobvious or unexpected results. *In re Rose* 220 F.2d. 459, 105 USPQ 237 (CCPA 1955).

***Response to Arguments***

In pages 4 and 5 of applicant's remarks, applicant argued that: (1) "the disclosure of the Piunno et al reference differs significantly." because the examiner's assertion and understanding "that $dA_{20}$ could be considered as a sample nucleic acid while $rA_{20}$ could be considered as a reference nucleic acid" is incorrect since "[T]he detected relative fluorescence intensify increased values are almost the same for $dA_{20}$ and $rA_{20}$, when the experimental errors are taken into consideration."; and (2) " [P]iunno et al is completely silent and contains no information with

respect to the differentiation between the fully complementary relationship to form a full match structure and the partly complementary relationship to form the mismatch structure." .

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, "[T]he detected relative fluorescence intensify increased values are almost the same for $dA_{20}$ and $rA_{20}$," did not affect that $rA_{20}$ served as a reference nucleic acid. Second, claims 1-20 did not require "the differentiation between the fully complementary relationship to form a full match structure and the partly complementary relationship to form the mismatch structure." . Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

***Conclusion***

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. No claim is allowed.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the patent Analyst of the Art Unit, Ms. Chantae Dessau, whose telephone number is (703) 605-1237.

Frank Lu
July 18, 2002

ETHAN C. WHISENANT
PRIMARY EXAMINER